Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (**Currently amended**) A method of identifying one or more ligand conformations that bind to a protein, the method comprising:

obtaining structural information for the protein and for one or more ligands;

identifying at least one binding region of the protein;

applying a coarse-grained docking algorithm to identify a plurality of binding conformations for the one or more ligands in the binding region;

selecting a set of best conformations by lowest energy from the binding conformations for the one or more ligands;

optimizing the best conformations using molecular mechanics;

further optimizing a subset of the best conformations by using annealing molecular dynamics ~~including~~ which incorporates solvation effects;

minimizing a preferred set of conformations from the subset of the best conformations;

calculating a binding energy for each conformation of the preferred set of conformations;

ranking the conformations of the preferred set of conformations based on the calculated binding energies;

selecting for each of the one or more ligands the conformation of the preferred set of conformations having the lowest calculated binding energy; and

outputting a data file comprising a list of selected ligand-protein conformations having the lowest calculated binding energy, and their respective binding energies;

wherein the method is performed by a programmable processor executing a program of instructions.

2. (Previously Presented) The method of claim 1, wherein the binding region is a known binding region.

3. (Canceled)

4. (Previously Presented) The method of claim 1, wherein the identifying at least one binding region of the protein comprises:

mapping empty volumes available for ligand binding in the protein to identify one or more potential binding areas;

generating initial conformations for one or more ligands known to bind the protein using a coarse-grained docking algorithm in each of the one or more potential binding areas;

calculating a value of a scoring function for the initial conformations;

selecting from the initial conformations for each of the known ligands a set of best conformations in each of the potential binding regions based at least in part on the value of the scoring function;

optimizing the conformations in the set of best conformations using molecular mechanics, thereby creating a set of optimized conformations each of which has a corresponding energy score; and

applying spatial clustering to a selection of the optimized conformations having the lowest energies, thereby identifying at least one binding region.

5. (Canceled)

6. (Previously Presented) The method of claim 4, wherein the selecting is further based on a calculated percentage of the ligand surface area buried within the protein for the conformation which exceeds a predetermined threshold.

7. (Canceled)

8. (Canceled)

9. (Previously Presented) The method of claim 1, wherein the annealing molecular dynamics uses a full atom force field.

10. (Previously Presented) The method of claim 1, wherein the solvation effects include a continuum description of solvation.

11. (Previously Presented) The method of claim 1, wherein the solvation effects include a surface-area based solvation model.

12. (Previously Presented) The method of claim 1, wherein calculating a binding energy for each conformation of the preferred set of conformations includes subtracting a free energy of the conformation in the protein from a free energy of the conformation in solution.

13. (Previously Presented) The method of claim 1, wherein the binding energy for a conformation of the preferred set of conformations is calculated according to a scoring function that comprises subtracting the free energy of the conformation in water from the energy of the conformation in the protein.

14. (Previously Presented) The method of claim 1, wherein the binding energy for a conformation of the preferred set of conformations is calculated according to a scoring function that comprises subtracting a sum of the free energy of the protein and a free energy of the conformation from a free energy of the conformation in the protein.

15. (Canceled)

16. (Previously Presented) The method of claim 1, wherein the protein is a globular protein or a transmembrane protein.

17-30. (Canceled)

31. (**Currently amended**) A computer program product for identifying one or more ligand conformations that bind to a protein, the computer program product comprising instructions operable to cause a programmable processor to:

obtain structural information for the protein and for one or more ligands;

identify at least one binding region of the protein;

apply a coarse-grained docking algorithm to identify a plurality of binding conformations for the one or more ligands in the binding region;

select a set of best conformations by lowest energy from the binding conformations for the one or more ligands;

optimize the best conformations using molecular mechanics;

further optimize a subset of the best conformations by using annealing molecular dynamics ~~including~~ which incorporates solvation effects;

minimize a preferred set of conformations from the subset of the best conformations;

calculate a binding energy for each conformation of the preferred set of conformations;

rank the conformations of the preferred set of conformations based on the calculated binding energies;

select for each of the one or more ligands the conformation of the preferred set of conformations having the lowest calculated binding energy i; and

output a data file comprising a list of selected ligand-protein conformations having the lowest calculated binding energy, and their respective binding energies,

wherein the computer program product is tangibly embodied in a machine-readable storage device for execution by a programmable processor.

32-35. (Canceled)

36. (Previously Presented) The computer program product of claim 31, wherein the instructions to identify at least one binding region of the protein comprise instructions to:

map empty volumes available for ligand binding in the protein to identify one or more potential binding areas;

generate the initial conformations for one or more ligands known to bind the protein using docking techniques in each of the one or more potential binding areas;

calculate a value of a scoring function for the initial conformations;

select from the initial conformations for each of the known ligands a set of best conformations in each of the potential binding regions based at least in part on the value of the scoring function;

optimize the conformations in the set of best conformations using molecular mechanics, thereby creating a set of optimized conformations each of which has a corresponding energy score; and

apply spatial clustering to a selection of the optimized conformations having the lowest energies, thereby identifying at least one binding region.

37. (Previously Presented) The computer program product of claim 31, wherein the annealing molecular dynamics uses a full atom force field.

38. (Previously Presented) The computer program product of claim 31, wherein the solvation effects include a continuum description of solvation.

39. (Previously Presented) The computer program product of claim 31, wherein the solvation effects include a surface-area based solvation model.

40. (Previously Presented) The computer program product of claim 31, wherein the instructions to calculate a binding energy for each conformation of the preferred set of ligands include subtracting a free energy of the conformation in the protein from a free energy of the conformation in solution.

41. (Previously Presented) The computer program product of claim 31, wherein the binding energy for a conformation of the preferred set of conformations is calculated according to a scoring function that comprises subtracting the free energy of the conformation in water from the energy of the conformation in the protein.

42. (Previously Presented) The computer program product of claim 31, wherein the binding energy for a conformation of the preferred set of conformations is calculated according to a scoring function that comprises subtracting a sum of the free energy of the protein and a free energy of the conformation from a free energy of the conformation in the protein.

43-44. (Canceled)

45. (Previously Presented) The computer program product of claim 31, wherein instructions to apply a coarse-grained docking algorithm to identify a plurality of binding conformations and select best conformations include instructions for: determining a percentage of the ligand surface area buried within the protein for each of the binding conformations; and determining energy scores for a portion of the best conformations, wherein each of the best conformations in the portion has a calculated percentage of the ligand surface area buried within the protein which exceeds a predetermined threshold.

46. (Previously Presented) The method of claim 1, wherein the calculating a binding energy for each conformation of the preferred set of conformations further comprises:

calculating a scoring function selected from the group consisting of:

(i) subtracting a free energy of the conformation in water from a free energy of the conformation in the protein; and

(ii) subtracting a sum of a free energy of the protein and a free energy of the conformation from a free energy of the conformation in the protein.

47. (Previously Presented) The computer program product of claim 31 , the computer program product further comprising instructions operable to cause a programmable processor to:

calculate a binding energy for each conformation of the preferred set of conformations according to a scoring function selected from the group consisting of:

(i) subtracting a free energy of the conformation in water from a free energy of the conformation in the protein; and

(ii) subtracting a sum of a free energy of the protein and a free energy of the conformation from a free energy of the conformation in the protein.

48. **(Currently amended)** A system for identifying one or more ligand conformations that bind to a protein, the system comprising:

a memory; and

a processor, wherein the processor is configured to execute instructions operable to:

obtain structural information for the protein and for one or more ligands;

identify at least one binding region of the protein;

apply a coarse-grained docking algorithm to identify a plurality of binding conformations for the one or more ligands in the binding region;

select a set of best conformations by lowest energy from the binding conformations for the one or more ligands;

optimize the best conformations using molecular mechanics;

further optimize a subset of the best conformations by using annealing molecular dynamics ~~including~~ which incorporates solvation effects;

minimize a preferred set of conformations from the subset of the best conformations;

calculate a binding energy for each conformation of the preferred set of conformations;

rank the conformations of the preferred set of conformations based on the calculated binding energies;

select for each of the one or more ligands the conformation of the preferred set of conformations having the lowest calculated binding energy; and

output a data file comprising a list of selected ligand-protein conformations having the lowest calculated binding energy, and their respective binding energies.

49. (Previously Presented) The system of claim 48, wherein the processor is further configured to execute instructions for calculating the binding energy according to a scoring function selected from the group consisting of:

(i) subtracting the free energy of the conformation in water from the energy of the conformation in the protein; and

(ii) subtracting a sum of the free energy of the protein and the a free energy of the conformation from the a free energy of the conformation in the protein.

50. (Previously Presented) The method of claim 1, wherein the annealing molecular dynamics uses an all atom forcefield selected from the group consisting of: AMBER, CHARMM, DREIDING, MMFF, and MM3.

51. (Previously Presented) The computer program product of claim 31, wherein the annealing molecular dynamics uses an all atom forcefield selected from the group consisting of: AMBER, CHARMM, DREIDING, MMFF, and MM3.

52. (Previously Presented) The system of claim 49, wherein the annealing molecular dynamics uses an all atom forcefield selected from the group consisting of: AMBER, CHARMM, DREIDING, MMFF, and MM3.

53. (Previously Presented) The method of claim 1, wherein the coarse-grained docking algorithm is a Monte Carlo algorithm.

54. (Previously Presented) The computer program product of claim 31, wherein the coarse-grained docking algorithm is a Monte Carlo algorithm.

55. (Previously Presented) The system of claim 49, wherein the coarse-grained docking algorithm is a Monte Carlo algorithm.

56. (Previously Presented) The system of claim 48, wherein the system is programmed to select the set of best conformations further based on a calculated percentage of the ligand surface area buried within the protein for the conformation which exceeds a predetermined threshold.